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13. ABSTRACT (Maximum 200 Words) The polyphenols, catechin, (-)-epigallocatechin-3-gallate (EGCG), genistein and resveratrol, are associated with reduced incidences of prostate and breast cancers. The goal of this research is to investigate the potential of these 3 pure polyphenols, alone and in combination, to protect against prostate cancer in an animal model that spontaneously develops prostate cancer (<u>TRAN</u> sgenic <u>MO</u> use <u>PRO</u> state adenocarcinoma (TRAMP)). In this manner, it may be possible to ingest moderate amount of each of these foods/chemicals, as opposed to mega amounts of one, and receive an additive or synergistic protective effect without adverse effects with possible elevated exposure. The specific aims are 1) to investigate the potential of genistein, EGCG and resveratrol, alone and in combination, to suppress the development of spontaneously developing prostate tumors and 2) to investigate the potential of genistein, EGCG and resveratrol to regulate sex steroid- and specific growth factor-receptor and ligand expression as mechanism of prostate cancer prevention. To date, the offspring were evaluated for transgene expression, and male TRAMP mice were subjected to these nutritional chemicals in AIN-76A diet or to control diet (AIN-76A), starting at 5 weeks postpartum. Each group contains 30 TRAMP males. Necropsy is scheduled for April - June 2004. Aim 2 has been initiated.				
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Introduction

Asians consuming a diet high in soy products have reduced incidence of clinically manifested prostate cancers. Likewise, Asians have a long history of drinking tea. Significant components of these two staples of the traditional Asian diet are the polyphenolic compounds. The primary polyphenols associated with prostate chemoprevention are the soy isoflavone, genistein, and the tea catechin, (-)-epigallocatechin-3-gallate (EGCG). Another polyphenol that has recently received attention as a cancer suppressor is resveratrol, a component of grapes. The goal of this research is to investigate the potential of these 3 pure polyphenols, alone and in combination, to protect against prostate cancer. In this manner, it may be possible to ingest moderate amount of each of these foods/chemicals, as opposed to mega amounts of one, and receive an additive or synergistic protective effect without adverse effects with possible elevated exposure.

Body

Aim 1) To investigate the potential of the polyphenols, genistein, EGCG and resveratrol, alone and in combination, to protect against prostate cancer. This is being evaluated in the TRAnsgenic Mouse Prostate adenocarcinoma (TRAMP) model that spontaneously develop prostate cancer. (Months 1-18)

Relying on preliminary data from mammary chemoprevention studies with genistein, EGCG and resveratrol in rats (an NIH supported study), where the low doses did not exert chemopreventive effects, we have concentrated on determining if single exposure to the proposed high doses of EGCG (0.06% in drinking water), resveratrol (625 mg/kg diet) and genistein (250 mg/kg diet), starting at 5 weeks of age, were going to be tolerated and result in suppressing prostate cancer development. C57BL/6 males and TRAMP females were bred and offspring have been produced. The offspring were evaluated for transgene expression, and male TRAMP mice were subjected to these nutritional chemicals in AIN-76A diet or to control diet (AIN-76A), starting at 5 weeks postpartum. Each group contains 30 TRAMP males. Necropsy is scheduled for April – June 2004. Following histopathological evaluation of the tumors by Dr. Isam Eltoum, we will decide if additional doses will be necessary. If these doses are appropriate for chemoprevention, we will initiate the combinational chemoprevention protocols.

Aim 2) To investigate the potential of genistein, EGCG and resveratrol to regulate sex steroid- and specific growth factor- receptor and ligand expression as mechanisms of prostate cancer prevention. From the dorsolateral prostates of mice exposed \pm polyphenols we will investigate expression of the androgen receptor (AR), estrogen receptors (ERs), epidermal growth factor receptor (EGFR), transforming growth factor-alpha (TGF-alpha), epidermal growth factor (EGF), insulin-like growth factor-I (IGF-I), IGF binding protein-3 (IGFBP-3), and extracellular signaling regulating kinases-1 and 2 (ERK-1 and ERK-2). (Months 18-36).

We have actually initiated this study. Mice are being bred and the offspring are being evaluated for transgene expression. Realizing that 2 mice/sample are insufficient to produce enough protein to measure all of the proteins proposed by western blot analysis, we are producing 3 mice for each sample, 8 samples/group. After we obtain the data of the single treatments, we will set up the combinational treatments.

Key Research Accomplishments

Except for the chemical treatments not having adverse effects on water and diet consumption, and on body weight, we have no data to report at this time.

Reportable Outcomes

None at this time.

Conclusion

Except for the chemical treatments not having adverse effects on water and diet consumption and on body weight, we have no conclusion to report at this time.